DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-427/S-009/S-011/S-013

Eli Lilly and Company
Attention: Dr. Ann R. Sakai, Ph.D.
Associate Director, Regulatory Affairs
Lilly Corporate Center
Indianapolis, Indiana 46285

Dear Dr. Sakai:

Please refer to your supplemental new drug applications dated January 23, 2006 (S-009), April 27, 2006 (S-011), and September 14, 2006 (S-013), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cymbalta® (duloxetine hydrochloride) 20 mg, 30 mg 40 mg and 60 mg tablets.

We acknowledge receipt of your amendments dated July 6, August 22, September 14 and 21, 2006 and January 24 and 25, 2007.

These supplemental new drug applications provide for the following revisions to product labeling;

S-009

1. Addition of a new subsection under **CLINICAL PHARMACOLOGY-Special Populations** entitled *Nursing Mothers*.
2. Revisions to the **PRECAUTIONS-Use in Patients with Concomitant Illness** subsection.
3. Revisions to the **PRECAUTIONS**-Nursing Mothers subsection.
4. Revisions to the **ADVERSE REACTIONS-Postmarketing Spontaneous Reports** subsection.
5. Revisions to the **OVERDOSAGE** section.
6. The addition of a new subsection under **DOSAGE AND ADMINISTRATION-Special Populations** entitled *Dosage for Nursing Mothers*.

S-011

- The addition of a new indication for the treatment of Generalized Anxiety Disorder (GAD).

S-013

- Revisions to the **ADVERSE REACTIONS-Postmarketing Spontaneous Reports** subsection.

We have completed our review of these applications, as amended, and they are approved, effective on the date of this letter, for use as recommended in the agreed upon and enclosed labeling text.

However, we note that the enclosed labeling also includes changes proposed in your pending "Changes Being Effected" supplemental application [redacted], dated August 9, 2005, and amended on October 17, 2005, and October 4, 2006. This supplemental application proposes the following revisions:

[redacted]

[redacted]. We are currently evaluating the revisions and will comment on the changes in a separate action letter.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text/submitted labeling. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, designate these submissions "FPL for approved supplement NDA 21-427/ S-009, S-011, S-013." Approval of these submissions by FDA is not required before the labeling is used.

Pediatric Research Equity Act (PREA) Requirements-Studies Deferred

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are waiving studies for ages 0 to 7 years (neonates and young children). We are deferring submission of your pediatric studies for ages 7 to 17 years (children and adolescents) until 3 years from the date of approval of this NDA.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of these postmarketing studies shall be reported annually according to 21 CFR 314.81. These commitments are listed below.

Post Marketing Commitments

1. Deferred Pediatric Studies Under PREA

You are required to assess the safety and effectiveness of duloxetine hydrochloride as a treatment for Generalized Anxiety Disorder in pediatric patients ages 7 to 17 (children and adolescents). Both children (ages 7 to 11) and adolescents (ages 12 to 17) should be equally represented in the samples, and there should be a reasonable distribution of both sexes in these age strata.

Final Report Submission: by February 28, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

2. Long-term Efficacy Study in Generalized Anxiety Disorder

Since GAD is a chronic illness, you are required to assess longer-term effectiveness and safety of duloxetine hydrochloride in GAD. You have agreed in your email submission dated February 9, 2007, to submit the results of one adult clinical study of duloxetine in the longer-term treatment of GAD. We note that you have an ongoing study that is expected to meet the requirements of this commitment.

Final Report Submission: by August 31, 2007

Please submit your final study report to the IND, clearly marked as "**Postmarketing Study Final Report**." If the study report is intended to support a change in labeling within this Division, please submit it to the NDA.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Psychiatry Product and two copies of both the promotional materials and the package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Felecia Curtis, Regulatory Project Manager, at (301) 796-0877.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren

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